Information Disclosure Statement upon receipt.

2. Rejection of claims 27-148 for obviousness-type double patenting

Applicants acknowledge the rejection of claims 27-148 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-63 of U.S. Patent No. 6,294,352. Applicants hereby elect to address this ground of rejection by submitting a Terminal Disclaimer, or by argument, upon notification that all other conditions for patentability have been met and the claims are otherwise in condition for allowance.

3. Objection to claims 132, 136, 137, 140-143, and 148 under 37 C.F.R. § 1.75(c)

The Office Action contains an objection to claims 132, 136, 137, 140-143, and 148 under 37 C.F.R. § 1.75(c) as being of improper form because a multiple dependent claim should refer to other claims in the alternative only, or cannot depend from any other multiple dependent claim.

Claim 132 has been amended so that it refers back to claim 97 alone. New claim 167, which corresponds to claim 132 and which refers back to claim 104 alone, has been added. Claims 136, 137, and 140-143 have been replaced by independent claims 168-173 and dependent claims 174-178. Claim 148 has been amended so that it refers back to claim 146 alone. New claim 178, which corresponds to claim 148 and which refers back to claim 147 alone, has been added.

Claims 114, 121, and 131 also appear to be in contravention of 37 C.F.R. § 1.75(c) as interpreted by the Examiner with regard to claims 132 and 148. Applicants have amended these claims so that each claim refers back to claim 97 alone. In addition, the following new claims have been added: (a) claim 149, which corresponds to claim 114 and which refers back to claim 104 alone, and dependent claim 150, which corresponds to claim 115; (b) claim 151, which corresponds to claim 121 and which refers back to claim 104 alone, and dependent claims 152-154, which correspond to claims 122, 123, and 128, respectively; and (c) claim 155, which corresponds to claim 131 and which refers back to claim 104 alone, and dependent claims 156-166 which correspond to claims 133-135, 138, 139, 144-148, and 178, respectively, have also been added.

Applicants contend that the claims, as amended, comply with 37 C.F.R. § 1.75(c), and therefore, respectfully request that this ground of rejection be withdrawn.

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4. Rejections of claims 41-48, 71-76, 78, 83-86, 89-91, 96, 97, and 104-148 under 35 U.S.C. § 112, second paragraph

The Office Action asserts a rejection of claims 41-48, 71-76, 78, 83-86, 89-91, 96, 97, and 104-148 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. The Action states that claims 41-48 and dependent claims 71-74, 76, 78, 83-86, 89-91, 96, 97, and 104-148 are indefinite because the phrase "at least one" in claims 41-47, 71, 72, and 74 does not put an upper limit on the extent of the changes to be made.

Applicants respectfully disagree with the assertion that claims 41-48 and dependent claims 71-74, 76, 78, 83-86, 89-91, 96, 97, and 104-148 are indefinite. Applicants contend that claims 41-47, 71, 72, and 74 contain an explicit limitation to encompass only those molecules that possess a particular activity, namely, the *ability to bind TNF*. The specification defines the "ability to bind TNF" as "the ability of a protein to bind to TNF-α in such a way that TNF-α is prevented from binding to the functional part of the receptor and the activity of TNF-α in humans or animals is inhibited or prevented altogether" (page 17, lines 23-28). Applicants respectfully disagree with the assertion made in the instant Action regarding the specie of substituted molecule having conservative substitutions at every amino acid position. The Action asserts that such a molecule could be made without destroying the ability of the resulting variant to bind TNF-α in such a way that TNF-α is prevented from binding to the functional part of the receptor and the activity of TNF-α in humans or animals is inhibited or prevented altogether. Applicants contend that they are under no duty to define, with absolute precision, the number of modifications that would be tolerable without destroying the ability of a molecule to bind TNF. Applicants also contend that the requirements of 35 U.S.C. § 112, second paragraph, are met because one of ordinary skill in the art would readily recognize that a molecule having conservative substitutions at *every* amino acid position would lack this high affinity TNF-α binding activity. Moreover, Applicants contend that 35 U.S.C. § 112, second paragraph, only requires that one of ordinary skill in the art would be able to determine which species fall within the scope of the claim (for example, by using the teachings of the specification at, *inter alia*, page 16, lines 28-31) in order for the claim language to be definite. Applicants, therefore, contend that claims 41-48 and dependent claims 71-74, 76, 78, 83-86, 89-91, 96, 97, and 104-148 satisfy the definiteness requirement of § 112, second paragraph, and respectfully request that this

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ground of rejection be withdrawn.

The Action also states that claim 75 is indefinite for reciting "[a] nucleic acid that hybridizes under moderately or highly stringent conditions," because specification does not define any hybridization conditions.

Applicants respectfully disagree with the assertion that the specification does not define any hybridization conditions. In fact, the specification discloses that cDNA clones containing TNF binding protein coding sequences were isolated from a fibrosarcoma cDNA library by hybridization for 16 hours at 65°C using a 0.4 kb probe isolated from the TNF-α induced fibrosarcoma cDNA library in a hybridization solution composed of 6x SSC, 5X Denhardt's, and 0.1% SDS (page 65, lines 17-28). However, in an effort to expedite prosecution of the instant application, Applicants have amended claim 75 to recite "[a] nucleic acid that hybridizes to the complement of the nucleic acid molecule of Claim 40 at 65°C in a hybridization buffer comprising 6x SSC and 0.1% SDS." Applicants contend that amended claim 75 satisfies the definiteness requirement of § 112, second paragraph, and therefore, respectfully request that this ground of rejection be withdrawn.

The Action also states that claim 132 is indefinite because there is no preamble describing the purpose of the method, and no method steps recited to achieve amplification. The Action further states that it is not clear what nucleic acid is to be amplified, since the host cell comprises endogenous nucleic acid molecules as well as the recombinantly introduced nucleic acid molecule.

Applicants have amended claim 132 so that it refers back to claim 131, which is drawn to a process of producing a recombinant polypeptide having the ability to bind TNF. Amended claim 132 also specifies that the amplified nucleic acid is the recombinantly introduced nucleic acid. Applicants note that claim 167, which corresponds to claim 132, has likewise been drafted so that it refers back to claim 155, which corresponds to claim 131, and specifies that the amplified nucleic acid is the recombinantly introduced nucleic acid. Applicants contend that amended claim 132 satisfies the definiteness requirement of § 112, second paragraph, and therefore, respectfully request that this ground of rejection be withdrawn.

In addition, Applicants note that claims 122 and 128 have been amended so that each claim properly refers back to claim 121, and that claims 124-127 have been amended to replace the phrase "eukaryotic cell," for which there appears to be no antecedent basis, with the phrase "recombinant host cell."

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Applicants respectfully contend that rejections based on 35 U.S.C. § 112, second paragraph, have been overcome by amendment or traversed by argument, and request that the Examiner withdraw all rejections made on this basis.

5. Rejections of claims 41-47 and 75 under 35 U.S.C. § 112, first paragraph

The Office Action asserts a rejection of claims 41-47 and 75 under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The Action states that the disclosure of a core polypeptide having a disclosed specific activity does not adequately support the scope of the claimed genus, which encompasses a substantial variety of species thereof.

Applicants respectfully disagree with the assertion that the specification fails to reasonably convey to one of ordinary skill in the art that the inventors had possession of the claimed invention at the time the application was filed. The specification sets forth the amino acid sequences of a TNF receptor polypeptide (page 5, lines 7-39) and a 161 amino acid portion of this sequence having the ability to bind TNF (page 5, line 45 to page 6, line 3). The specification also discloses that the first 29 amino acid residues of the TNF receptor polypeptide constitute the signal peptide (page 21, line 35 to page 22, line 2), and that amino acid residues 30-40 and 202-211 are proteolytically cleaved from the TNF receptor to form the TNF binding protein (page 22, lines 11-12 and page 23, lines 27-29). The specification teaches that techniques for making conservative substitutions are well known in the art (page 14, lines 13-15), and provides a list of exemplary conservative substitutions (page 15, Table 1). Applicants contend that they are under no duty under the statute to enumerate all of the species disclosed generically in their specification, particularly where, as here, the structure of the native molecule is disclosed, the types of variants of said structure are generically disclosed, and a functional property of the claimed molecule (TNF binding activity) and assays to assess species for said property are disclosed. The specification also teaches the location of glycosylation sites (page 22, lines 16-19), proteolytic cleavage sites (page 22, lines 26-28 and page 23, lines 27-29), and cysteine residues (SEQ ID NO: 2), wherein amino substitutions can be made. Applicants, therefore, contend that the specification conveys to one of ordinary skill in the art that the inventors had possession of the claimed invention, and request that this ground of rejection be withdrawn.

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CONCLUSIONS

Applicants respectfully contend that all conditions of patentability are met in the pending claims as amended. Allowance of the claims is thereby respectfully solicited.

If Examiner Andres believes it to be helpful, she is invited to contact the undersigned representative by telephone at (312) 913-0001.

Respectfully submitted,
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Dated: November 18, 2002

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AMENDMENTS TO THE CLAIMS

Marked Up Versions of Amended Claims under 37 C.F.R. 1.121(c)(1)(ii)

75. (Amended) A nucleic acid that hybridizes ~~under moderately or highly stringent conditions~~ to the complement of the nucleic acid molecule of Claim 40 at 65°C in a hybridization buffer comprising 6x SSC and 0.1% SDS.

114. (Amended) The recombinant host cell of ~~either~~ Claims 97 ~~or 104~~, wherein the recombinant host cell is a prokaryotic cell.

121. (Amended) The recombinant host cell of ~~either~~ Claims 97 ~~or 104~~, wherein the recombinant host cell is a eukaryotic cell.

122. (Amended) The recombinant host cell of Claim ~~104~~ 121, wherein the eukaryotic cell is a mammalian cell.

124. (Amended) The recombinant host cell of Claim 106, wherein the ~~eukaryotic cell~~ recombinant host cell is a Chinese Hamster Ovary cell.

125. (Amended) The recombinant host cell of Claim 108, wherein the ~~eukaryotic cell~~ recombinant host cell is a Chinese Hamster Ovary cell.

126. (Amended) The recombinant host cell of Claim 110, wherein the ~~eukaryotic cell~~ recombinant host cell is a Chinese Hamster Ovary cell.

127. (Amended) The recombinant host cell of Claim 112, wherein the ~~eukaryotic cell~~ recombinant host cell is a Chinese Hamster Ovary cell.

128. (Amended) The recombinant host cell of Claim ~~104~~ 121, wherein the

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eukaryotic cell is a yeast cell.

131. (Amended) A process of producing a recombinant polypeptide having the ability to bind TNF comprising culturing the recombinant host cell of ~~either~~ Claims 97 ~~or 104~~ under suitable conditions to express the polypeptide.

132. (Amended) ~~A~~ The process of claim 131, further comprising culturing the recombinant host cell ~~of either Claims 97 or 104~~ under suitable conditions to amplify the recombinant nucleic acid molecule.

148. (Amended) The process of ~~either~~ Claim 146 ~~or 147~~, wherein said recovered polypeptide is formulated to comprise said polypeptide and a pharmaceutically acceptable carrier.

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